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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,814	07/05/2001	Francisco Javier Garcia-Ladona	0480/001210	1323

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,814	GARCIA-LADONA, FRANCISCO JAVIER	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-32 and 34-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-32 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment in filed on 24 November 2003 is acknowledged and entered. Following the amendment, claims 19-28 and 33 are canceled, and the new claim 36 is added.

Currently, claims 29-32 and 34-36 are pending and under consideration.

The declaration under 37 CFR 1.132 filed on 24 November 2003 is acknowledged, and it is insufficient to overcome the following rejection of claims 29-35 based upon lack of enablement under 35 U.S.C. 112, first paragraph, for the reasons below.

The data presented in the declaration demonstrates that the compound HK02-01 of the present invention significantly decreases spreading velocity in the experiment of retinal spreading depression, which, according to applicants, is a well-recognized model for evaluating the efficacy of compounds in the treatment of migraine (Fernandez de Lima, V.M. et al., Brain Res., 1993, 614:45-51, cited by applicants). However, the Examiner is not able to locate, nor to extract from the Fernandez de Lima reference that retinal spreading depression is a well-recognized model for evaluating compounds in the treatment of migraine. Additionally, applicants indicate in the declaration that a compound significantly decreasing spreading velocity is expected to be effective in the treatment of migraine, and the compound HK02-01 significantly decreases spreading velocity. This is not deemed persuasive because the art has not established that spreading velocity is a predictable indicator that necessarily correlates to the effectiveness of a compound on migraine even though some effective compounds such as Sumatriptan decreases spreading velocity, and present specification provides no guidance nor working examples to support such a correlation.

Nonetheless, prior art search by the Examiner reveals that spreading depression is associated with migraine aura, and may play a role in triggering classical migraine. As such, treating migraine aura would be considered enabling even though it remains unclear whether the compound is effective on migraine headache or the entire condition of migraine.

Withdrawal of Objections and Rejections:

All objections and rejections of claim 33 are moot as the applicant has canceled the claim.

The rejection of claims 29-32, 34 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

The rejection of claims 29-32, 34 and 35 under 35 U.S.C. 112, first paragraph, for total lack of enablement, made in the last Office Action is withdrawn in view of applicant's declaration, and the reasons addressed above.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a method for treating migrainous cerebrovascular disorders using the compound HK02-01, does not reasonably provide enablement for claims to a method for treating migrainous cerebrovascular disorders using any or all binding partner for a 5-HT5 receptor with binding affinity indicated in those claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 29-36 are directed to a method for treating migrainous cerebrovascular disorders such as migraine with *binding partners* for a 5-HT5 receptor, which reads on any or all compounds binding to a 5-HT5 receptor. The declaration filed on 24 November 2003 merely provides *one* of such binding partners, the compound HK02-01, and no other binding partners for 5-HT5 receptor meeting the limitations of the claims were ever identified or particularly

described. Additionally, the specification provides no instruction/guidance or working example regarding how to make all binding partners for 5-HT5 receptor, which are suitable for the treatment. Further, the art has not established that any binding partner for a receptor would be effective for therapy, i.e., merely binding of a compound to a receptor cannot be used to predict the biological effect of the compound. A binding partner for 5-HT5 receptor can be an agonist or an antagonist of the receptor, which would be mutually exclusive with respect to their therapeutic application, and it seems, according to the specification, that it is the agonist of the receptor effective for the treatment. Therefore, the specification does not reasonably provide enablement commensurate in scope with claims, and it would require undue experimentation to practice the invention in a manner commensurate in scope with the claims.

Due to the large quantity of experimentation necessary to identify all binding partners for a 5-HT5 receptor, which meet the functional limitations of the claims, the lack of direction/ guidance presented in the specification regarding to how to make same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art that has not established that the binding to a receptor is a sufficient indicator for therapeutic applications, and the breadth of the claims which embrace both agonist and antagonist, undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 29-36 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As addressed above, with the exception of the compound HK02-01, no other binding partners for 5-HT5 receptor meeting the limitations of the claims were ever identified or particularly described. It is required that the patent specification set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In a recent case law, *University of Rochester, v. G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc.* (03-1304), the Court recites from *In re Ruschig*, 379 F.2d 990 (CCPA 1967):

> [T]he appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. . . . A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its function of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. [Regents of the Univ. of Cal. v.] Eli Lilly [& Co., Inc.], 119 F.3d [1559,] 1568 [(Fed. Cir. 1997) ("Lilly")] . . . . The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Id.

The Court further states that "regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods. As the district court observed, "[t]he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment." Id."

In the instant situation, with the exception of the compound HK02-01, the present specification does not disclose the structure or physical properties of any additional compounds encompassed by the claims, and required to practice the claimed methods, and that the structure of such compounds cannot be deduced from any known structure-function correlation, even considering the knowledge of one skilled in the art.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the compound HK02-01, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
2/12/04